

**P13** Effect of Annual Influenza Vaccine on the Immunologic Response in the Elderly

R. Rüttimann,<sup>2\*</sup> H. S. Izurieta,<sup>1</sup> R. C. Arduino,<sup>2</sup> N. Arden,<sup>1</sup> F. Nacinovich,<sup>2</sup> A. Montepiedra,<sup>1</sup> I. Escribano,<sup>2</sup> H. Hall,<sup>1</sup> P. Bonvehi,<sup>2</sup> H. Regnery,<sup>1</sup> D. Stambouljan.<sup>2</sup>  
<sup>1</sup>Centers for Disease Control and Prevention, Atlanta, GA; <sup>2</sup>Fundación del Centro de Estudios Infectológicos, Buenos Aires, Argentina

Although annual influenza vaccination is recommended for persons aged  $\geq 65$  years, little is known about the long-term effect of repeated annual vaccination on the immunologic response in this population. To assess this effect, we recruited subjects aged  $\geq 65$  years during an influenza vaccination campaign in Buenos Aires in April 1996.

Volunteers provided a blood specimen at the time of vaccination and 3-4 weeks later and answered questions about previous influenza vaccinations, chronic medical conditions, and current medications. Sera were tested for hemagglutination-inhibition antibody titers to each of the 3 strains in the 1995-96 influenza vaccine.

Among 165 subjects, 67 (41%) had no previous influenza vaccination, 58 (35%) had one, and 40 (24%) had  $\geq 2$ . There were no statistically significant differences in age or chronic conditions among the groups. Postvaccination (PV) geometric mean titers (GMTs) of antibodies to each of the vaccine antigens were highest among the group that had received one previous influenza vaccination and lowest among the group that had received  $\geq 2$ . The magnitude and direction of our findings did not change when data were stratified by age or chronic diseases. PV-GMTs among healthy participants were up to 60% higher than among those who had chronic diseases but were not significantly different among age groups. Seventy-three to 95% and 64%-86% of subjects from all groups had PV titers  $\geq 1:40$  and  $\geq 1:80$ , respectively, which have been previously correlated with protection, depending on the antigen tested.

These findings support the recommendation for annual vaccination of persons aged  $\geq 65$  years.

**P15** Efficacy and Effectiveness of Inactivated Influenza Vaccine Among Children Attending Day Care

E. S. Hurwitz,<sup>\*</sup> A. Chang, M. Hoerber, T. Shope, S. Teo, CDC, San Diego State University; Emory University; San Diego Naval Medical Center and County Health Department

During the 1996-97 influenza season, a blinded randomized controlled trial was conducted among children 24-60 months of age attending day care centers to evaluate the efficacy and effectiveness of influenza vaccine. A total of 145 children matched for age were enrolled from 10 large day care centers and randomized to receive influenza (74 children) or hepatitis A vaccine (71 children) as a placebo. Serologic response to vaccine was evaluated via hemagglutination inhibition (HI) antibody; influenza infections were identified based on four-fold titer rises to HI during the influenza period. Clinical illness data was obtained via telephone interviews conducted with parents every 2 weeks. Surveillance for influenza demonstrated influenza A(H3N2) and B activity during the influenza period; among controls tested, 16% (8/51) had influenza A(H3N2) and 43% (22/51) had influenza B infection. Vaccine efficacy in preventing infection was 0.45 (95% CI=0.05-0.70). For both influenza A(H3N2) and B, children who had prevaccination antibody were more likely to develop a serologic response to vaccine which was protective against infection. Although there was no vaccine effectiveness against influenza-like illnesses (ILIs) during the 14-week influenza period, cluster analysis demonstrated effectiveness against ILIs in those with influenza B infections during the first 6 weeks (vaccine effectiveness [VEF]=0.82,  $p=0.03$ ), which was significantly greater than that during the last 8 weeks (VEF=0.11,  $p=0.36$ ) ( $p<0.005$ , first 6 vs. last 8 weeks). Children attending day care appear to be at high risk of influenza infection. Those with prior influenza infections are more likely to develop a vaccine response which is protective against infection. Larger studies are needed to further define the efficacy and effectiveness of influenza vaccine in these children.

**P14** Effect of Prior Vaccination on Antibody Responses to Inactivated Influenza Vaccine in Years When Vaccine Components Change and in Years Without a Change in Vaccine Components

J. J. Treanor,<sup>\*</sup> D. O'Brien, S. Wu, D. Vosefski, R. Battaglia, R. F. Betts, University of Rochester, Rochester, NY

**Objectives:** There continues to be occasional concern regarding the effect of annual immunization on the response to influenza vaccine, particularly in years when the vaccine formulation does not change. The objective of this study was to compare the effect of prior vaccination both in years when the vaccine formulation changed and when it did not.

**Methods:** A total of 97 healthy adults received a single dose of licensed trivalent inactivated influenza vaccine intramuscularly in two studies conducted in sequential years, and the serum antibody response was determined by hemagglutination-inhibition. Data was analyzed by the subject's self-reported vaccine history.

**Results:** During the two year interval, each of the strains of the trivalent vaccine was changed once. A history of prior vaccination was associated with a significantly decreased frequency of antibody responses to the H1 and B components in the year that those strains were changed. Rates were also somewhat lower in previously vaccinated subjects in the year when the components did not change, but the differences in rates were not statistically significant. There was no effect of prior vaccination on the rate of response to the H3 component in either year. Prior vaccination either had no effect (H3 viruses) or increased slightly (H1 and B viruses) the proportion of individuals achieving protective titers to each of the three components of the vaccine in both years.

**Conclusions:** These data generally support the policy of annual vaccination with inactivated influenza vaccine.

**P16** Neonatal Group B Streptococcal Disease: Progress Towards a Multivalent Maternal Vaccine

L. C. Paoletti,<sup>\*</sup> C. J. Baker, D. L. Kasper, Channing Laboratory, Brigham & Women's Hospital, Harvard Medical School, Boston, MA; Baylor College of Medicine, Houston, TX

Group B *Streptococcus* (GBS) is the leading cause of bacterial sepsis and meningitis among neonates, and is also responsible for morbidity in women during parturition. Protective immunity is targeted to the GBS capsular polysaccharide (CPS) antigens. As vaccine scandidates, purified CPS antigens failed to elicit protective levels of CPS type specific antibody in nonimmune adults, a finding that led to the development of conjugate vaccines. Our goal is to develop a pentavalent GBS vaccine to the five serotypes most often encountered in U.S. populations. A safe GBS conjugate vaccine given to women at 30 to 32 weeks of gestation could result in protection against GBS infection in both mother and infant. Preclinical testing, and phase 1 and phase 2 clinical trials in adult, non-pregnant women (n=420, 11 trials) have been accomplished with conjugate vaccines of serotypes Ia, Ib, II, III, and V. Tetanus toxoid was used as the carrier protein for all CPS because of its well-documented history of safe use in pregnant women. CRM<sub>197</sub> was also used successfully as a carrier protein for GBS type V CPS. Overall, conjugate vaccines were well-tolerated with minimal reactivity. Significant rises in type-specific IgG were observed 2 weeks after vaccination and each conjugate elicited higher levels of antibody to CPS compared to the equivalent dose of uncoupled CPS. Based on results from dose-response studies and estimates of the level of protective immunity, a pentavalent GBS conjugate vaccine formulation is proposed.